Role of neuregulin-1β in dexamethasone-enhanced surfactant phospholipid synthesis in rat fetal type II pneumocytes *

G KING,[1] G L MAKER,[1†] D BERRYMAN,[1] R D TRENGOVE,[2] & M H CAKE[1]

[1] *School of Veterinary and Life Sciences, Murdoch University, Murdoch, WA 6150, Australia.*

[2] *Separation Science and Metabolomics Laboratory, Murdoch University, Murdoch, WA 6150, Australia.*

[†] *Corresponding author* ✉ *G.Maker@murdoch.edu.au*

Surfactant production is known to involve a cellular communication between lung fibroblasts and the type II pneumocytes. Glucocorticoids induce the production of a peptide by lung fibroblasts, fibroblast-pneumocyte factor (FPF), which sequentially acts on type II cells to enhance the synthesis of surfactant phospholipid. Our findings show that fibroblast-conditioned medium (FCM), generated in the presence of dexamethasone, not only enhanced surfactant phospholipid synthesis in type II cells but also contained an elevated concentration of neuregulin-1β (NRG1β). Even though it has been earlier proposed that leptin has many of the characteristics of FPF, recent research has revealed that NRG1β also has many similar atributes. In the current study, exposure of the type II cells to a commercially available form of NRG1β (heregulin-1β) directly stimulated by more than three-fold the rate of phospholipid synthesis ($p < 0.05$). Although similar in magnitude, the effect of heregulin-1β appeared to require a longer time of exposure to that reported for leptin. There was no increase in the gene expression of NRG1β when lung fibroblasts were exposed to dexamethasone, irrespective of the concentration of dexamethasone used, or the time of contact of the cells to the steroid. Thus the glucocorticoid-induced increase in the level of NRG1β in FCM was not the result of enhanced expression of the NRG1β gene. The inability of dexamethasone to induce a significant increase in NRG1β gene expression in lung fibroblasts suggests that the elevated concentration of NRG1β might be the result of enhanced cleavage of the membrane-bound neuregulin precursor. In summary, these findings not only support but significantly extend the concept previously promoted that NRG1β plays an essential role in the differentiation and maturation of the lung in the later stages of gestation. Moreover, together these studies suggest that FPF may be a complex mixture of agents capable of motivating surfactant synthesis.

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